

Attorney's Docket No.: 07043-015007  
Client's Ref. No.: B92-011-6

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : M. Allen Northrup et al.      Art Unit : 1634  
Serial No. : 08/900,735      Examiner : Sisson, B.  
Filed : July 24, 1997  
Title : MICROFABRICATED REACTOR

Assistant Commissioner for Patents  
Washington, D.C. 20231

DECLARATION OF WILLIAM J. EGAN, III

I, William J. Egan, III, hereby declare and state that:

1. I am a principal with the law firm of Fish & Richardson P.C., and attorney of record for Applicants in this matter. I am a member in good standing and registered to practice before the United States Patent and Trademark Office. I have personal knowledge of the facts contained in this declaration and can competently testify to them.

2. During the time frame of just before May 1, 1992 to August 31, 1992, I was a principal with the law firm Heller, Ehrman, White & McAuliffe ("Heller"). Also during this time frame, Lawrence J. Shaw ("Mr. Shaw") was a registered patent agent who worked with me at Heller, and who was involved in the preparation of the parent of the subject application. The parent application was filed on August 31, 1992 and issued as U.S. Patent 5,639,423 on June 17, 1997.

CERTIFICATE OF MAILING BY FIRST CLASS MAIL

I hereby certify under 37 CFR §1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

January 5, 2000  
Date of Deposit

Bridget Conger  
Signature

BRIDGET CONGRER  
Typed or Printed Name of Person Signing Certificate

3. We exercised due diligence in this country in preparing and filing the parent application from the period extending from prior to May 1, 1992 to August 31, 1992, as evidenced by the following:

- On April 8, 1992, I had a telephone conference with Scott A. Taper, Jr. ("Mr. Taper") of the Office of Technology Licensing ("OTL") at the University of California, Berkeley regarding preparation of the parent application. Subsequently, on April 9, 1992, I spoke with Dr. M. Allen Northrup ("Dr. Northrup"), one of the inventors of the subject matter of the application, regarding its preparation. Specifically, we discussed the fact that we would prepare an outline of the application, which would be expanded on later in a future meeting with Dr. Northrup (Exhibit A).
- On May 11, 1992, I met with Dr. Northrup and Professor Richard M. White ("Prof. White"), the other inventor of the subject matter of the application. During the meeting, we discussed the content of the application as well as a schedule for the preparation of a draft of the application and a date by which we hoped to file it (Exhibit B, which includes notes of that meeting).
- On June 2, 1992, a rough draft of the parent application was faxed to Dr. Northrup and Prof. White. A copy of this draft was also sent to Mr. Taper (Exhibit C).
- After receiving the inventors' comments on the draft of June 2, 1992, the application was revised, and the revised draft was sent to Dr. Northrup and Prof. White on July 8, 1992 (Exhibits D and E).

Applicant : M. Allen Northrup et al.  
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Page : 3

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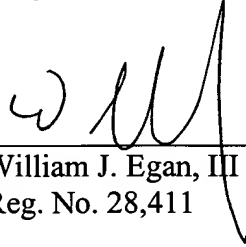
- Thereafter, the application was again revised and that draft of the application was sent via Federal Express on August 28, 1992 to Dr. Northrup and Prof. White (Exhibit F).
- On August 31, 1992, the application was filed in the U.S. Patent and Trademark Office. A copy of the filed application was sent to Mr. Taper, Dr. Northrup, and Professor White on the same day (Exhibit G).

4. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and that such willful false statements may jeopardize the validity of the application or any patents issuing thereon.

Respectfully submitted,

Date: \_\_\_\_\_

1/5/00

  
\_\_\_\_\_  
William J. Egan, III  
Reg. No. 28,411

WJE/mxj

Fish & Richardson P.C.  
2200 Sand Hill Road, Suite 100  
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Telephone: (650) 322-5070  
Facsimile: (650) 854-0875

#15

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : M. Allen Northrup et al.

Art Unit : 1634

Serial No. : 08/900,735

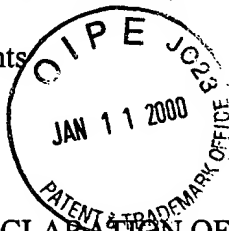
Examiner : Sisson, B.

Filed : July 24, 1997

Title : MICROFABRICATED REACTOR

Assistant Commissioner for Patents

Washington, D.C. 20231



EXHIBITS FOR DECLARATION OF WILLIAM J. EGAN, III

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Signature

BRIDGET CONGAR  
Typed or Printed Name of Person Signing Certificate

A

## TELEPHONE/PERSONAL CONFERENCE MEMO

Date 4/9/92 Time \_\_\_\_\_

Place \_\_\_\_\_

Conference with \_\_\_\_\_

Telephone: To \_\_\_\_\_  
From S. Taper (4/8)Confirmation: Dr Northrup (4/9)  
Required ExpectedFile No. 18043-0021Client UCB

Matter \_\_\_\_\_

Attorney WJZ

Discussion Dr. Northrup's phone # is 510-422-1638  
will submit an Abs. on 5/23/92 for  
show, which is set for 7/21-7/25/92.  
Abs, according Northrup, will not be  
pub. until a date of show, ie 7/21.  
Abs is keep confid until then.

we will prep an outline of the app  
& plan to meet w/ Northrup to  
dis app further & flush  
in w/ details that he has.

Memo Copy to \_\_\_\_\_

Signed \_\_\_\_\_

1

B

5/11/92

①

Key features:

BSAC

PCR or thermal-cycle driven  
enzymatic reactions, but  
includes other DNA (or  
other biochem or chem) reactions

All techns. involving reaction-based  
methodologies

Ability to integrate elec, mech  
or optical comp's. using micro-fab  
techs:

Reaction parameter control: heating,  
pumping, circulating, cooling

Reaction or reagent detection-manipulation

WTR Appl. depicted Fig. 2 chamber &  
specific sys. for carrying out  
PCR reactions. What are  
minimum comp's. of such a system?

Detect: mass change, density, viscosity  
Bio chem reaction manip, control & detection: ① chamb-wave  
devices - to pp, mix & detect;  
② electrokinetic effects to pp,  
sys or precanc; ③ interg-T<sup>o</sup>  
control devices; ④ optical filters  
⑤ chamber w/ heating elements



C

HELLER, EHRMAN, WHITE & McAULIFFE  
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June 2, 1992

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WRITER'S DIRECT DIAL NUMBER  
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18043-0021

Scott A. Taper, Jr.  
Licensing Associate  
University of California at Berkeley  
Office of Technology Licensing  
2150 Shattuck Avenue, Suite 510  
Berkeley, CA 94704

Re: U.S. Patent Application for  
Microfabricated Reactor

Dear Mr. Taper:

Enclosed is a copy of the rough draft of the patent application which was faxed to M. Allen Northrup and Richard M. White on June 2, 1992.

Very truly yours,

Heller, Ehrman, White  
& McAuliffe



Carol Sowards  
Secretary to Laurence J. Shaw  
Registered Patent Agent

LJS:cls  
enclosure

ATT

Allen Northrup

Dick White

5/11/92

thermal cycling

claim: mixing chamber; also  
 claim system.

micro liter vials  $\rightarrow$  used in system  
 smaller — can be done faster  
 w/ less power.

96  $\leftrightarrow$  550C  $\rightarrow$  heat & cool.

system on

Re-packaged/chips  $\rightarrow$  novel:  
 integ. on chips.

chem. or bio-chem

\* PCR or any other reaction that  
 requires thermal cycling.

Monolithic, microFab device  $\rightarrow$   
 1st time such a sys  
 has been done on this scale.

use of hand-wheel as  
moves particles in single

\* <sup>file</sup> chip to see if I have  
file on white's us  
5,006, 149.

unifex: microheaters in chamber  
key part of inv. / system.

Fiber optic inside reaction chamber  
for detection.

PCR techs now take about <sup>1 to 5 minutes</sup> ~~1 to 5 minutes~~  
~~of inv. can get results in~~  
~~1 to 5 minutes.~~ Fastest is  
micro. in time. ~ can get  
results in a few seconds.  
re cycles on the order of  
a cycle. Due to small  
vols & high surface area.  
could be portable & work w/  
batteries as opposed to 110V.

~~to diff. x surface x~~  
Reactions dep. on concentration  
\* 3 volts in chamber & work in seconds

on  $\rightarrow$  3 volts in  $96^{\circ}\text{C}$  based on heater Res.  
 off  $\rightarrow$  1/2 volts in  $55^{\circ}\text{C}$  " "

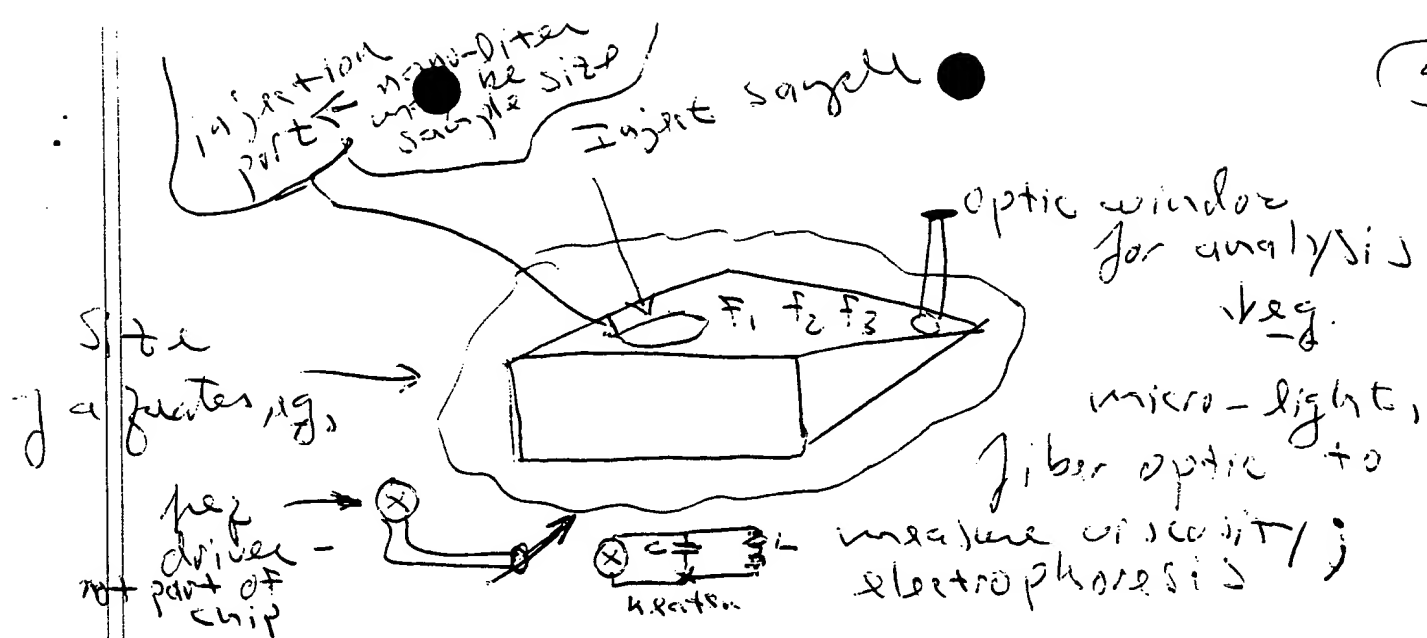
Monolithic Forb — is very important  
 — can do in batches on  
 wafers. Thus they are  
 cheap & are disposable.

\* Need spec sheet for chamber  
 fabrication

Ppling in chamber — re Dick  
 white

Chamber — includes ultrasonic  
 agitator for mixing.

$\downarrow$  Also useful for cell dispensing



pump, mixer etc run  
a diff pres ( $F_1, F_2, F_3$ ) so  
can turn diff components on & off  
by opening a diff pres.  
Heating is also done by turning  $F_4$   
in heater.

Key doing PCR on chip w/  
reaction chamber.

~~Materials~~ Materials used in chamber  
can negatively effect PCR  
reactions eg. Buffer  
divalent cations will prevent  
PCR from being.

Reactants on chip in advance  
& sold as a unit.

Use of surface tension to maintain reactants  
in reactant container.

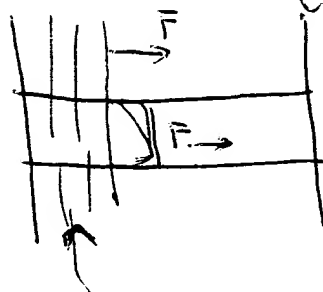
Possible talks / pubs : none on  
the horiz; Oct 1992

Draft appl to Inverters by bagling  
to mid-June & file by end  
of June

\* Remote drive

Ads: All parts of channels moved at  
same speed - adv. of carb-  
vane PP.

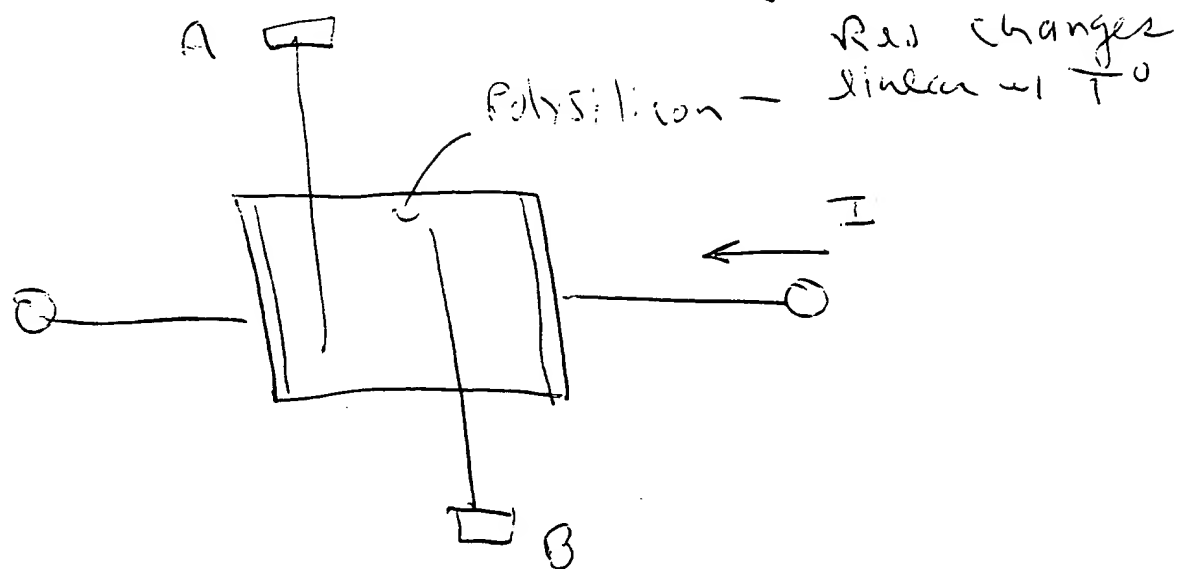
dee whiters  
WS 5,006, 749



Blunt Flow  
- more solid

Lamb-wave  
generators

$T^0$  control  $\rightarrow$  Nice feature.



Use ~~less~~ <sup>electrodes</sup> A + B to measure  $T^0$  change. Send in known current  $I$  + measure voltage bet. electrodes A + B.

This detail should be in log.



$\text{SiO}_2$  - is material at bottom  
of chamber; std material  
handled by bio-chemists

DNA probes - in chamber;  
parts attach to probes + detector  
change so know have attachment  
to probes.

7

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July 8, 1992

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18043-0021

M. Allen Northrup, Ph.D.  
Engineering Research Division  
LAWRENCE LIVERMORE NATIONAL LABORATORY  
P.O. Box 808  
Livermore, California 94551

Re: U.S. Patent Application  
MICROFABRICATED REACTOR

Dear Allen:

Enclosed please find the latest draft of the above-referenced patent application, as well as the previous draft with your comments. Please give me a call after you review the document.

Very truly yours,

Heller, Ehrman, White  
& McAuliffe

*Laurence J. Shaw*  
Laurence J. Shaw  
Registered Patent Agent

LJS:cls  
Enclosures  
cc: William J. Egan, III (w/o encl)

E

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WRITER'S DIRECT DIAL NUMBER

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18043-0021

Professor Richard M. White  
Berkeley Sensor and Actuator Center  
497 Cory Hall  
UC Berkeley  
Berkeley, California 94720

Re: U.S. Patent Application  
MICROFABRICATED REACTOR

Dear Richard:

Enclosed please find the latest draft of the above-referenced patent application, as well as the previous draft with your comments. Please give me a call after you review the document.

Very truly yours,

Heller, Ehrman, White  
& McAuliffe

*Laurence J. Shaw/cls*  
Laurence J. Shaw  
Registered Patent Agent

LJS:cls  
Enclosures  
cc: William J. Egan, III (w/o encl)

F

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18043-0021

2672211640

VIA FEDERAL EXPRESS

2672211651

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M. Allen Northrup  
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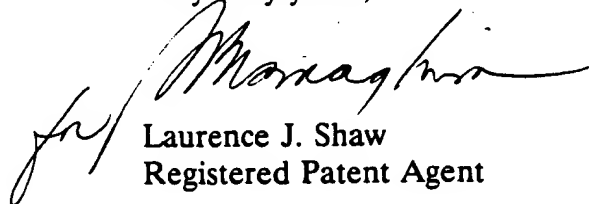
Re: U.S. Patent Application  
MICROFABRICATED REACTOR

Gentlemen:

Enclosed for your review is the latest draft of the above-identified patent application. This application incorporates the changes and suggestions made to date.

This application is to be filed on Monday, August 31. Please contact me on Monday morning with your comments, if any.

Very truly yours,

  
Laurence J. Shaw  
Registered Patent Agent

Enclosures  
cc: William J. Egan, III (w/o enc,)

G



HELLER, EHRMAN, WHITE & MCAULIFFE  
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August 31, 1992

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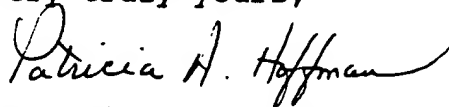
Scott A. Taper, Jr.  
Licensing Associate  
University of California at Berkeley  
Office of Technology Licensing  
2150 Shattuck Avenue, Suite 510  
Berkeley, CA 94704

Re: U.S. Patent Application for  
Microfabricated Reactor

Dear Mr. Taper:

Enclosed is a copy of the subject patent application  
which was submitted to the U.S. Patent and Trademark Office for  
filing today.

Very truly yours,



Patricia A. Hoffman  
Secretary to Laurence J. Shaw  
Registered Patent Agent

enclosure

cc: M. Allen Northrup (w/encl. and original photo)  
Richard M. White (w/encl.)  
William J. Egan, III (w/encl.)